IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Applicant:

PECKER et al

Serial No.: 10/785,116

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Group Art Unit: 1652

For: Polynucleotide Encoding A Polypeptide Having Heparanase Activity And Expression of Same in Genetically Modified Cells

Examiner: R. Hutson

Attorney Docket: 27674

Commissioner for Patents
P. O. Box 1450
Alexandria VA 22313

DECLARATION UNDER 37 U.S.C. SECTION 1.131

Sir:

I, Iris Pecker, declare as follows:

1) I am the Iris Pecker who is an inventor named in the above-identified subject invention.

2) I have analyzed the alignment data shown in Figure 17 of the subject application. In my opinion, it provides ample guidance to the skilled artisan on how to make active heparanase variants. For example, residues 77 to 98 of mouse heparanase (SEQ ID NO:44) are identical to the corresponding residues of the variants shown in Figure 17. By contrast, for example, residues 15 to 28 have 11 residue differences. Similarly, comparing mouse and human heparanase, residues 129 to 138 (referring to the reside positions in human), for example, have 9 of 10 differences at this region. With such guidance, the skilled artisan would know to

not vary residues 77 to 98 and to vary one or more residues among residues 15 to 28 and/or 129 to 138, especially with a similar amino acid residue substitution (e.g., hydrophilic). The skilled artisan could even further use the guidance of the subject specification to replace one or more amino acid residues in SEQ ID NO:44, especially in these highly variable regions, with those corresponding residues found in human or rat heparanase.

3) Looking at heparanase protein more broadly, residues 49 to 109 (referring to human) make up 61 residues. Comparing mouse and human region in this region, there are only 10 of 61 changes. Comparing mouse and rat in this region, there are only 6 of 61 changes. This is therefore a very conserved region, one that the skilled artisan would likely not vary, at least as a starting point, in trying to obtain additional heparanase homologs.

4) The conserved region of residues 49 to 109 was confirmed to be the 8 kDa unit of active heparanase. By contrast, variable regions 15 to 28 and 129 to 138, discussed in paragraph 2 above, are not part of either the small or large units of mature heparanase.

5) Moreover, Figure 19 of the subject application provides even further guidance. Figure 19 shows the secondary structure prediction for heparanase using computer assistance. The portions depicted as "H" are helical, and the portions depicted as "E" are extended beta strand structures.

6) Still further, the glutamic acid residue of heparanase, predicted as the proton donor, is marked with an asterisk in Figure 19. Given the relative location of the proton donor and the predicted secondary structure of the protein, the glutamic acid residue that functions as the nucleophile is most likely at position 343 or 396 (see underlined residues in Figure 19, and page 105, lines 20-22 of the subject specification).

7) Given the wealth of information in the subject specification, the skilled artisan can make heparanase variants without undue experimentation.

I declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willfully false statements are punishable by fine or imprisonment under 18 U.S.C. Section 1001 and that any such statement may jeopardize the validity of the subject application or any patent issued thereon.

Iris Pecker

Dr. Iris Pecker

7/12/06

Date